UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/690,353	10/16/2000	Douglas A. Collins	COP1003	2345

7590 06/03/2002

Sherry M Knowles
King & Spalding
191 Peachtree Street NE
45th Floor
Atlanta, GA 30303

EXAMINER
JONES, DAMERON LEVEST

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 06/03/2002 16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/690,353	COLLINS ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1616	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2001 and 06 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 October 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

APPLICANT'S INVENTION

1. Applicant's invention is directed to cobalamin conjugates and uses thereof.

112 REJECTIONS

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

w/a Claims 17, 28, 32, and 33: The claims as written are ambiguous because it is unclear where the linkage of the residue occurs. Formula I (Figure 1) does not appear to have a valence available for the linkage. Applicant is respectfully requested to clarify the claim in order that one may readily ascertain what is being claimed.

w/ b Claims 17(line 3), 28 (line 3), and 32 (line 4): The claims are ambiguous because it is unclear what 'suitable carboxy protecting group' Applicant is intending to be compatible with the instant invention.

Claims 1-69: The claims as written are confusing because they are directed to Formula I (Figure 1) wherein there are some questions regarding the attachment of w/ c some atoms as well as whether there are too many attachments to a carbon atom, for example. In particular, in Formula I (Figure 1) the –CH2OH group appearing in the lower right-hand corner is not attached to the five-member oxygen containing ring.

Also, the double bonded X group is questionable. In particular, the specification defines X as CN, OH, CH3, or adenosyl; however, it is not structurally possible to have =CN, =OH,=CH3. In addition, the CO4 group appearing in the center of the structure should be Co4, not CO4. Also, in section g of the structure, Applicant has CH2-CONH2-CH3-C (attaches to the carbon of ring A). The attachment of CH2-CONH2-CH3-C is impossible since there are too many attachments to the CH3 group. Furthermore, the attachment of the single bond to the five-membered ring of section D is confusing because it is unclear where the bond is connected to the structure. As a result of the confusing structure (Formula I), Applicant is respectfully requested to thoroughly examine the structure and determine if it accurately depicts what is being claimed.

Claims 1-69: The claims as written are ambiguous because one cannot readily ascertain what is being claimed. In particular, the second paragraph of 35 USC 112 requires that the claims particularly point out the subject matter that Applicant regards as the invention. However, the claims refer to a figure (Figure 1) that contain a variable, X, that one must search the specification for a definition. Thus, according to Ex Parte Fressola, 27 USPQ 2d 1608 (US Patent & Trademark Bd. Pat. App. & Int., 1993) is improper except in rare instances. Hence, in an effort to clarify the claims so that one may readily ascertain what is being claimed, Applicant is respectfully requested to insert Formula I and a definition for the variable X1, n, DET, and Q in the appropriate claims.

Claim 33, line 3: The residue is ambiguous because it is unclear whether Applicant intended the variable Rj to be attached to the 4-position or if Applicant intended it as a variable point of attachment (Rj may be attached anywhere on the six-

membered ring). Applicant is respectfully requested to clarify the residue in order that one may readily ascertain what is being claimed.

Claims 56-69: The claims as written are confusing because (1) the claim form is improper because a multiple dependent claim cannot depend on other multiple dependent claims and (2) it is unclear what claim(s) Applicant actually intended the claims to depend upon.

Claims 64-69 provide for the use of the cobalamin compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

DOUBLE PATENTING

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 28-33, 35-37, 40-45, and 56-69 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-15 of U. S. Patent No. 6,211,355. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a compound comprising a linker, chelator, and cobalamin group.

6. Claims 60-69 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U. S. Patent No. 6,096,290. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of treating a tumor with a vitamin B12 compound.

7. Claims 28-30 and 56-69 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U. S.

Patent No. 5,739,313. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a vitamin B12 compound comprising linker, chelator, cobalamin group, and a metallic radionuclide and uses thereof.

8. Claims 28, 29 and 56-69 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 10 of U.S. Patent No. 6,004,533. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a compound comprising a linker, chelator, and cobalamin group, and radionuclide or paramagnetic metal and uses thereof.

9. Claims (1-69), (28 and 56-59), (1-69), (1-69), (28-32), (28-32), and (1-69), respectively, are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims (1, 3-6, 12, 13, 15, 16, 18, 19, and 21-23), (1, 12, 15, 16, 18, 19, and 22), (1, 3, 17-25, 29-32, 35, 69, 70, and 72-74), (1, 49, 56-59, 62, 69-73, and 105), (1-14 and 19-23), (128, 29, 31, 32, 39, and 40), and (1, 28, 29, 31-35, 39, 45, 47, and 48), respectively, of copending Application No. 10/027,593; 10/028,857; 09/690,197; 09/690,198; 09/626,213; 09/873,142; and 09/873,164, respectively. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to vitamin B12 derivatives and uses thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

101 REJECTIONS

10. Claims 64-69 are is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

102 REJECTIONS

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 28-32 and 56-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins et al (WO 97/18231).

Collins et al disclose the radionuclide labeling of vitamin B12 and coenzymes thereof. In addition, the reference discloses (1) the compound is useful for in vivo imaging of organs and tumors; (2) the compound comprises a linking group and a chelating group; (3) the compound optionally comprises a detectable radionuclide or a

paramagnetic metal ion (see entire document, especially, abstract). The chelating agent may be DTPA, EDTA, DCTA, DOTA, or TETA (page 5, lines 6-8; pages 6-7, bridging paragraph). (4) Possible detectable labels include Tc-99m, In-111, and Gd-153 (page 5, line 8; pages 8-9, bridging paragraph; page 16, lines 6-8; pages 16-17, bridging paragraph; page 17, lines 3-6; page 17, Example 9; page 19, Table II; pages 23-25, claims 1-25).

Thus, both Collins et al and Applicant disclose compounds of Figure I having a chelator, linking group, and a metallic radionuclide.

13. Claims 49-51 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Niswender et al (US Patent No. 3,981,863).

Niswender et al disclose cyanocobalamin derivatives which may be iodinated to introduce 125I or 131I into one or both of the two positions of the phenolic group ortho to the hydroxyl group (see entire document, especially, abstract; column 2, lines 40-46). In addition Niswender et al disclose (1) proteins such as polylysine may be covalently bonded with vitamin B12 (column 3, lines 1-9) and (2) procedures for incorporating 125i and 131I (column 4, Examples 7 and 9).

Thus, both Niswender et al and Applicant disclose a vitamin B12 compound having a non-metallic radionuclide.

103 REJECTIONS

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-11 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niswender et al (US Patent No. 3,981,863).

Niswender et al (see discussion above) fails to disclose the attachment of a peptide to its radiolabeled vitamin B12 complex.

w/d It would have been obvious to one of ordinary skill in the art at the time the invention was made to generated a compound of Figure 1 comprising a peptide and radionuclide because the reference (column 3, lines 1-8) disclose that the vitamin B12 may be covalently bonded to polylysine.

15. Claim 49 is rejected under 35 USC 103(a) as being unpatentable over Bernstein et al (US Patent No. 4,209,614).

Bernstein et al disclose the radiolabeling of vitamin B12. In particular, vitamin B12 may be labeled with a radioisotope such as 125I or 131I (see entire document, especially, abstract; column 3, lines 29-44). While Bernstein et al disclose the w/ s radiolabeling of a vitamin B12 derivative with iodine, the reference fails to disclose a structure having Applicant's Figure 1.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Bernstein et al and generate a compound

of Figure 1 labeled with iodine because the prior art discloses that it is known in the art to label vitamin B12 and derivatives thereof with iodine.

16. Claims 1-11, 16, 20, 21, 24, and 47-56 are rejected under 35 USC 103(a) as being unpatentable over Morgan et al (WO 97/14711).

Morgan et al disclose vitamin B122 compounds and methods thereof wherein the compounds are comprised of a covalently bound rerouting moiety and a targeting moiety linked by a water solubilizing linker (see entire document, especially, abstract; pages 13-14, bridging paragraph; pages 17, lines 28-33; column 20, lines 7-11). In addition, Morgan et al disclose (1) the rerouting moiety may be assessed by employing a receptor modulating agent having a radiolabeled targeting moiety (page 21, lines 10-13). (2) The rerouting peptides may be covalently attached to a targeting moiety by any means such as covalently linking a peptide directly to the targeting moiety (page 24, lines 8-11; page 36, lines 6-25). (3) A vitamin B12 complex may be conjugated to a radioisotope and used for radiodiagnostic or radiotherapeutic purposes (page 38, lines 12-16). While Morgan et al disclose that a vitamin B12 derivative may be radiolabeled, the reference fails to disclose specific radiolabels that may be attached.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Morgan et al and generate a vitamin B12 derivative that may be labeled with both metallic and non-metallic radionuclides because the reference does not limit the radionuclide to any specific ones, but generally

teaches the radiolabeling of the vitamin complex for radiodiagnostic or radiotherapeutic purposes.

SPECIFICATION

17. The disclosure is objected to because of the following informalities: some of the text appearing at the top of pages 2-20, 22, 24, 25, and 27-35 is not readable. Thus, Applicant is respectfully requested to submit clean copies of each page.

Appropriate correction is required.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (703) 308-4640. The examiner can normally be reached on Mon.-Fri. (alternate Mon.), 6:45 a.m. - 4:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose' Dees can be reached on (703) 308- 4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

D. L. Jones
Primary Examiner
Art Unit 1616

May 29, 2002